Report to ASCEPT for travel grant-funded attendance at IUPHAR 2006

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Thanks to the generosity of ASCEPT, and the award of an ASCEPT travel grant, I was able to travel to Beijing, China at the start of July 2006, to attend the IUPHAR World Congress in Pharmacology. The program for the conference had a wide range of seminars that either directly related to my PhD project, or were of interest in terms of broadening my general knowledge of pharmacology. Those seminars that were of direct interest and their resulting impact upon the direction of my project are as follows:

‘Spatial and temporal controls of PKC isoform activation’ Yasuhito Shirai
This presentation focused upon the time to activation or translocation of a number of PKC isoforms. This time varies between isoforms, and also within a single isoform depending upon the stimulus involved. This is highly relevant to my current work, as an element of the cAMP signalling pathways of the H2 relaxin receptor involves the activation and translocation of PKCζ. We, and others, have demonstrated that this occurs in a delayed manner following receptor stimulation, thus this presentation provides a potential mechanism for this phenomena, and evidence to support our data.

‘Structure and organization of GPCRs’ Graeme Milligan
Presented evidence not only for the formation of dimers between receptors, but also for the linking of dimeric or oligomeric receptor complexes to forms chains of receptors. This had previously been demonstrated for rhodopsin receptors, but now also for other receptor types. This presentation also introduced a number of new techniques (including the use of FRET between three proteins, instead of the usual two), which were of potential future interest for my PhD project.

‘Crosstalk in GPCRs: changes at the transmembrane homodimer interface determine activation’ Jonathan Javitch
This seminar examined the regions of receptors which are involved in dimerisation and the consequential movement of the receptors themselves to allow dimerisation to occur. Again, this was of particular relevance to my project, as the receptors I am studying have a high potential for dimerisation. The presentation also used the model of receptor dimerisation presented to provide evidence for different receptor dimerisation conformations induced by full vs partial vs inverse agonists etc.

‘Targeting protein-protein interactions in signalling pathways for therapeutic interactions’ Haian Fu
This seminar focused upon a protein called 14-3-3 which binds to other phosphorylated proteins and allows interaction or activation of additional signalling molecules. Again, this was of high interest and relevance to my project, as we are currently attempting to identify differences between H2 relaxin and INSL3 receptors, which are related to their differing abilities to activate cAMP signalling. One of the possibilities was the presence of a potential 14-3-3 binding motif in one receptor but not the other.

‘Modular assembly of GPCR signalosomes’ Michel Bouvier
This was a very interesting presentation which again looked at receptor dimerisation. Evidence was presented for the activation of different signalling pathways for heterodimeric vs homodimeric vs single receptors. The use of different BRET and FRET

techniques has enabled the examination of specific interactions between receptor and G proteins, between G protein subunits, and between G proteins and interacting proteins such as GRKs. This work has implications for our accepted understanding of the receptor-G protein-signalling molecule interactions.

In addition to seminar attendance, I presented a poster of a component of my PhD project entitled ‘Differential G protein coupling of the relaxin family peptide receptors, RXFP1 and RXFP2, is due to differences in the C-terminal tail’. This allowed helpful discussion of my work with Dr Changlu Liu from Johnson & Johnson, US, Prof Steve Hill from Nottingham, UK and Dr Rochdi Bouhelal from Novartis, Switzerland. Some interesting suggestions and comments were made, which I will take into consideration in future experiments.

Overall IUPHAR 2006 was a very interesting and informative conference to attend. My attendance at this conference would not have been possible without the award of an ASCEPT travel grant.